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Jean-Jacques Caboche

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EXAMINER

OLSON, ERIC

ART UNIT

PAPER NUMBER

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/030,002	Applicant(s) CABOCHE ET AL.	
	Examiner ERIC S. OLSON	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-24 and 31-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-24 and 31-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on February 10, 2009 and April 10, 2009 have been entered.

Detailed Action

This office action is a response to applicant's communication submitted February 10, 2009, wherein claims 19, 31, and 38 are amended, and Applicant's communication submitted April 10, 2009, wherein claim 31 is amended and new claims 39-44 are introduced. This application is a national stage application of PCT/FR00/01109, filed April 26, 2000, which claims priority to foreign application FR99-05523, filed April 30, 1999.

Claims 19-24 and 31-44 are pending in this application.

Claims 19-24 and 31-44 as amended are examined on the merits herein.

Applicant's amendment, submitted February 10, 2009, with respect to the rejection of claims 19-22 and 38 under 35 USC 103(a) for being obvious over Okada et al. in view of Senkeleski et al., has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to require that the branched

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glucose polymer comprise an additional chain of glucose units at every 10-14 glucose units. Therefore the rejection is withdrawn.

The following new grounds of rejection are introduced:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-37 and 3-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). In the present instance, claims 31, 34, 39, and 42 recite the broad recitation between 2.5 and 10% of α -1,6 glucosidic bonds, and the claim also recites "wherein said soluble branched polymers of glucose in isolated and purified form comprise, at every 10 to 14 glucose units, an additional chain of glucose units," which is the narrower statement of the range/limitation. This narrow range of one side chain every 10 to 14 glucose units would, as the branching enzyme introduces side chains as α -1,6 bonds, indicate that the branched starch contains between about 6.7 and 9.1% α -1,6 glucosidic bonds, which is significantly narrower than the broad limitation recited in said claims.

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Furthermore the dependent claims 32, 36, and 37 insert additional limitations that limit the amount of α -1,6 glucosidic bonds of 2-5-5% or 5-10%. Both of these ranges similarly include embodiments outside of the range of 6.7-9.1%, and therefore lack antecedent basis in the base claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-24 and 31-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment submitted February 10, 2009 with respect to the aforementioned claims has been fully considered and but is deemed to insert **new matter** into the claims since the specification as originally filed does not provide support for the limitation that the soluble branched polymers of glucose in isolated and purified form comprise at every 10 to 14 glucose units an additional chain of glucose units. As the instant specification as filed contains no description of this limitation the specification as originally filed does not provide support for the subject matter of instant claims 19-24 and 31-44. See *in re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972).

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The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-24 and 39-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method involving certain specific branching enzymes, for example from *E. coli*, *C. reinhardtii*, or maize, does not reasonably provide enablement for a method utilizing any possible starch branching enzyme whatsoever expressed in any genetically modified expression system whatsoever. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

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Nature of the invention: The claimed method is an *in vitro* biocatalytic reaction involving a purified enzyme. In order to use the claimed invention, one skilled in the art must possess the branching enzyme.

The state of the prior art: Various starch branching enzymes are known in the art from various organisms. In fact, these enzymes are common across a wide variety of species due to the ubiquity of starch as a storage medium. Some of these enzymes have been cloned and recombinantly expressed, and are useful for modifying the properties of starch *in vitro*. For example, enzymes from maize, *Bacillus megaterium*, and *Chlamidomonas reinhardtii*, have been isolated in this manner. However, the prior art does not reveal the isolation of each and every possible starch branching enzyme, or of a representative sample thereof.

Furthermore, while certain expression systems such as *E. coli*, yeast, or mammalian cell culture are well known in the art for expressing recombinant proteins, the prior art does not reveal the full scope of all possible genetically modified organisms that could be used to express an exogenous protein such as a starch branching enzyme.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: Discovering new genes in new organisms is an unpredictable task. Although one skilled in the art would have reason to suspect that many organisms possess an as yet undiscovered starch branching gene, finding that gene in the genomes of a wide variety of plants and microorganisms

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would involve difficult and unpredictable experimentation. Furthermore, the expression and purification of an enzyme, which is necessary in order to use it in the claimed method, is also difficult and unpredictable. According to Short Protocols in Molecular Biology, Third Edition, (Reference of record in previous action) bacterial expression systems have several disadvantages, including lack of post-translational modification, formation of inclusion bodies, and inadequate excretion from the cell. Mammalian and baculoviral expression systems can overcome some of these disadvantages but are more difficult and time-consuming and are not adequate for the large-scale production of proteins. Each new starch branching enzyme would require further experimentation to determine the best method for expression and purification before it could be used in the claimed method.

Furthermore, in order to use any “genetically modified organism capable of expression said enzyme,” one skilled in the art would have to develop a wide variety of recombinant expression systems involving a large number of unrelated organisms and tissue cultures. This process would be highly unpredictable as many organisms are not well characterized and their suitability for protein expression is not known.

Therefore the process of obtaining every starch branching enzyme would be highly unpredictable.

The Breadth of the claims: The claimed invention is very broad, encompassing all starch branching enzymes. There is no particular limitation on the species from which the enzyme is extracted or its structural or physical properties.

The amount of direction or guidance presented: The claimed specification suggests the use of certain existing starch branching enzymes. In addition, a general strategy is suggested for the use of polyclonal antibodies to discover new enzymes related to existing algal starch branching enzymes.

The presence or absence of working examples: The working examples provided use one specific enzyme, obtained from *Chlamidomonas reinhardtii*.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the discovery, purification, and expression of new enzymes. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the full scope of the invention with every possible starch branching enzyme, one skilled in the art would have to identify a vast range of different enzymes, and express and purify them in a form suitable for use. Because the prior art does not teach expression and purification of every possible enzyme, many of these techniques would have to be developed from scratch. Although some of these enzymes have been successfully used for *in vitro* biocatalysis, finding optimal expression and purification methods for all of the remaining enzymes would be difficult and unpredictable as discussed above. Furthermore, using all possible genetically modified organisms as expression systems would provide an equally great and unpredictable burden of experimentation. Therefore practicing the full scope of the invention would require an undue burden of unpredictable experimentation.

Genentech, 108 F.3d at 1366, states that, “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion.” And “patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.”

Therefore, in view of the Wands factors, as discussed above, particularly the lack of guidance or working examples and the unpredictability of the art, Applicants fail to provide information sufficient to practice the claimed invention for all possible enzymes and expression systems.

Response to Argument: Applicant’s arguments, submitted April 10, 2009, with respect to the above ground of rejection have been fully considered and not found persuasive to remove the rejection. Applicant argues that branching enzymes are a conventional reagent in the art, just like any other chemical reagent. However, branching enzymes differ from chemical reagents such as hydrochloric acid in that the term refers to a broad range of different compounds having a certain effect, while a chemical term such as hydrochloric acid refers to a single chemical entity that is identical no matter what its source. Different enzymes from different species, on the other hand, will be vastly different in their activity, selectivity, stability, and other properties. By applicant’s own admission, “branching enzyme” refers not to a particular structure or sequence but to a technical effect. By merely reciting the technical effect of the enzyme rather than a particular sequence, source, or structure, Applicant has failed to limit the scope of the claims to enzymes that would in fact be accessible to one skilled in the art. For these reasons the rejection is deemed proper and maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 19-22 and 31-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okada et al. (US patent 4454161, of record in previous office action) in view of Senkeleski et al. (US patent 5562937, of record in previous action) in view of Sandström et al. (PCT international publication WO95/22562, of record in previous action, also published as Brynolf et al. (US patent 5929052, of record in previous action)

Okada et al. discloses a branched alpha-glucose polymer (starch) produced by the activity of a branching enzyme, for example an animal, plant, or microorganism branching enzyme in a starch such as amylopectin. (column 1 lines 47-63) A gelatinized solution of the starch is subjected to the action of the branching enzyme and then used, after concentration and/or drying, in food products. (column 2, lines 5-20) A bacillus branching enzyme is reported (column 5, lines 15-23) having an optimal temperature of about 25C and being stable up to about 45C. (column 6 lines 39-49) an *E. coli* branching enzyme is also reported. (column 8 lines 1-25) These starches display a reduced propensity for retrogradation. (column 2, lines 21-31) Okada et al. does not disclose a method in which the starch is gelatinized by a treatment at over 130°C and 3.5 bars as recited in the instant claims. Okada et al. also does not explicitly disclose a

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method in which the amount of branching enzyme is between 50-2000 units and the reaction is carried out at exactly 30°C. Okada et al. does not disclose a composition having a branch point at every 10-14 glucose units, or one having the molecular weight, percent of alpha 1,6 bonds, or reducing sugar content recited in the instant claims.

Senkeleski et al. discloses a method for digesting waxy starch with beta-amylase. (column 1, lines 40-58) The starch, in order to be processed in this manner, is first steam cooked at a temperature of 120°C to 170°C at a pressure of 60-80 psi, which is equivalent to about 4.1-5.5 bar.

Sandström et al. discloses a branched starch (alpha-glucose polymer) having a molecular weight ranging from 1.5×10^4 to 10^7 daltons, corresponding to the limitations in instant claim 31. (p. 3, lines 16-24) These starches have a branching degree of about 2-8%, preferably 3-7%. (p. 4, lines 1-3) A starch with this molecular weight will possess less than 1% reducing sugars, as there will be only one reducing end per molecule. The starch is particularly stable in solution, (p. 2 lines 25-31) and will therefore have a low tendency to retrograde in solution. These molecules are also considered to possess the claimed viscosity of at most 5000 cP in view of the fact that they possess the same structural characteristics (size, degree of branching) as those described in the instant specification. (for example p. 21, table II of the instant specification) It is noted that the starches of Sandström et al. differ from the claimed invention in that they possess beta-glycosidic linkages as a result of the specific method of acid treatment used to increase the branching degree.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the method of Okada et al. in view of Senkeleski et al. to produce a branched product as described by Sandström et al., having the same molecular weight and degree of branching but lacking beta-glycosidic bonds. One of ordinary skill in the art would have recognized that the enzymatic treatment of Okada et al. in view of Senkeleski et al. produces the same result, namely increased branching, as the acid treatment of Sandström et al., and that the two treatments are therefore interchangeable. With regard to the presence of beta-glycosidic bonds in the compounds of Sandström et al., this structural feature is an incidental result of the particular acid treatment used, and is not seen to be necessary for the desired properties, namely stability and reduced osmolality, present in the starches of Sandström et al. One of ordinary skill in the art would reasonably have expected success because the method of Okada et al. in view of Senkeleski et al. is already seen to be useful for increasing the branching degree of a starch.

Furthermore, it would have been obvious to one of ordinary skill in the art to optimize the various characteristics of the starch of Sandström et al., such as degree of branching and molecular weight, to arrive at the values discussed in instant claims 32, 36, and 37. One of ordinary skill in the art would have been able to choose optimal values for these experimental parameters through a simple process of routine optimization, and would clearly have recognized these structural properties to be result-effective variables that could be varied to produce the desired solution properties in the final product. Note that the new limitation that the branched polysaccharide have a

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branch point at every 10-14 glucose units is equivalent to a composition of between 6.7-9.1% α -1,6 bonds, considering that naturally occurring, enzymatically synthesized starches are polymers of α -1,4 bonds with branch points of α -1,6 bonds.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted April 10, 2009, with respect to the above ground of rejection have been fully considered and not found persuasive to remove the rejection. Applicant merely reiterates the arguments made in the after final response of February 10, 2009, which are not found to be persuasive for reasons set forth in the advisory action of February 26, 2009. Therefore the rejection is deemed proper and maintained.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. OLSON whose telephone number is (571)272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
7/1/2009